**Genomic epidemiology of infectious diseases**

EMD 531, Spring 2020

Course Instructor: Nathan Grubaugh (nathan.grubaugh@yale.edu)

TF: TBD

Office hours: Tuesdays 3:00-4:30 pm, LEPH 608

Course meetings times: Tuesdays & Thursdays, 10:00-11:20 am

Course location: LEPH 115

**COURSE DESCRIPTION**

Due to several factors, such as climate change, urbanization, and globalization, pathogens are continuing to emerge at an alarming rate. During these rapidly unfolding outbreaks, several questions need to quickly answered. *1*) What is the pathogen and what do we know about it? *2*) Where did it come from and when did it get here? *3*) What are the transmission dynamics and how do we stop transmission? We can answer many of these questions using pathogen genomics, especially when integrated into traditional epidemiological investigations.

This course will serve as an introduction to the use of genomic epidemiology for studying the cause, source, and dynamics of infectious disease infections and outbreaks. Topics that will be covered include the logistics of sequencing, bioinformatics and phylogenetics, real-world applications, and the critical review of case studies.

The course will primarily consist of lectures and student presentations that are meant to stimulate thoughtful discussions of the subjects. There will be some practical exercises in which students will gain experience aligning genomes and generating phylogenetic trees. **No previous experience is necessary**, though familiarity with molecular biology and phylogenetics would be helpful. This video provides a nice introduction to the subject:

* https://www.coursera.org/lecture/hkuepidemics/video-2-3-phylogenetics-5JlPG

**PRE-REQUISITES**

* Principles of Infectious Diseases I or equivalent microbiology/infectious disease course
* OR permission from the instructor

**COURSE OBJECTIVES**

By the end of the course students will be able to:

1. Understand the basic principles of how microbial evolution can be used to study epidemiology.
2. Understand the laboratory and computational workflows from sequencing to phylogenetics.
3. Perform multiple sequence alignments and maximum likelihood phylogenetic tree reconstructions.
4. Analyze genomic and phylogenetic data to answer fundamental questions about infectious disease infection, transmission, and spread.
5. Evaluate outbreak scenarios to apply appropriate genomic epidemiological approaches.
6. Evaluate case studies to identify methods to improve, draw public health conclusions, and communicate the results to the public.

**COURSE WEBSITES:**

* Canvas (lectures, readings, exercises)
* Github (practice data): <https://github.com/grubaughlab/EMD531_Gen-Epi-Inf-Dis>

**ACADEMIC INTEGRITY** <http://publichealth.yale.edu/about/gateways/students/MPH/capi.aspx>

[Students are required to adhere to the Yale School of Public Health Code of Academic and Professional Integrity](http://publichealth.yale.edu/about/gateways/students/MPH/capi.aspx). Failure to adhere to the Code can result in penalties as severe as dismissal.

Honor Code:

Upon completion of all written examinations, students will be asked to sign the following statement:

*I have not given, received, or witnessed inappropriate exchange of information on this assignment, and I certify that this is my own original work.*

**COURSE REQUIREMENTS**

1. Class attendance: Attendance is required. Please contact both instructor and the TA **at least 12 hours before a session** if you are unable to attend.
2. Class participation: Participation in class discussions is both expected and evaluated. Each student is expected to complete the readings and exercises prior to class.

**ADDITIONAL COURSE EXPECTATIONS**

1. Computers in the classroom: Laptop computers are allowed in the classroom, and will be needed for the in-class exercises. However, please do not check email and surf the internet during class.
2. Readings and exercises: Complete all of the readings prior to class. The exercises will all be due before spring break, but there is an expectation that you will keep up with the exercises to help you be prepared for class. There is a lot of material to cover, and getting behind will hinder your ability to participate in class activities and discussions.
3. Group learning: Support the learning of your classmates through in-class participation and group activities.
4. Communication: Please email the instructor or TA if you have any questions. If they are questions about the exercises, we expect that you will at least try to resolve the issue independently before emailing. If you have questions that require more than a brief response, attend office hours or make an appointment to speak with the TA or course instructor.

**WHAT CAN YOU EXPECT FORM US?**

1. We (instructor and TA) will make every effort to treat all students fairly and equitably regarding course expectations.
2. We will inform you of readings, assignments, presentations, and exams in a timely fashion.
3. We will respond to your emails and brief questions promptly.
4. We will be available during our respective office hours to answer questions.

**READING MATERIAL**

1. PDF copies of all reading materials will be provided.

**SOFTWARE**

Please download these free software programs listed in the exercises prior to class. Please attend office hours before this class if you need help downloading the programs.

**STUDENT EVALUATIONS**

Grading scale: All grades will be out of 100 and rounded to 1 significant figure.

* 88.0 to 100: Honors
* 78.0 to <88.0: High pass
* 68.0 to <78.0: Pass
* <68.0: Fail

Grade breakdown will be as follows:

* Participation: 25%
* Exercises: 25%
* Presentation: 25%
* Final exam: 25%
* \*\*Each will be out of 100 points, and I’ll take the average of the 4 to determine the final grade.

**READINGS AND ACTIVITIES**

There are a lot of reading assignments for this class to give you background information to allow us to cover more material during the lectures. Some of this information is expected to be discussed during class and will be needed for the final exams.

In-class group activities are meant to promote critical and creative thinking about current challenges in genomic epidemiology. This will contribute towards your participation grade. If you miss a group activity, you will be asked to complete a brief assignment on the topic.

**CLASS PARTICIPATION**

Genomic epidemiology in an evolving and complex field, with many real-world challenges. Some of these cannot be taught through traditional lectures, but rather by discussing as a class or in small groups. This is the reason why participation in class will make up 25% of your grade. You will start with 100 points and will maintain those points for as long as you participate in (1) class activities, (2) discussion of exercises, and (3) case studies discussions. 5 points will be deducted for each event for which you are not prepared (you will be notified via email from the instructor after class). Points for missed class can be made up at the discretion of the instructor.

*\*\*If you have any reason why speaking in class or groups will be difficult for you, please notify me ASAP. We will provide alternative means for you to participate.*

**EXERCISES**

The exercises are meant to provide hands-on experience working with genetic data. The exercises are due the class before spring break and will be graded for accuracy. Discussion about the exercises will also contribute to your participation grade. Completion of the exercises and accompanying questions will be worth 100 points (20 for each of the 5 exercises). See separate documents explaining the exercises and points for more details.

*\*\*These exercises require working with many different genetic software programs, text editors to modify script, and (light) command line. We will try to provide instructions and tutorials to make this approachable for all students. However, if you are struggling, please notify us ASAP.*

**PRESENTATIONS**

You will work individually or with a small group to present a genomic epidemiology paper to the class. Each presentation should be ~30 minutes, including time for discussion. Please see the separate document about the presentations for more details. One grade, up to 100 points, will be given to the group or individual. Up to 75 points will be given based on your presentation of the five assigned topics/questions (15 points each), 10 points for overall organization, and 15 points for facilitating discussion and answering questions. A detailed score sheet will be handed out before presentations and we’ll discuss this in class.

**FINAL EXAM**

The final exam will be take-home and must not be discussed with peers. For part 1, you will be given pathogen genomic data and will be asked to generate and annotate a phylogenetic tree. Then, you will be asked to describe your approaches and answer specific questions about the outbreak using the tree. For part 2, you’ll be presented with cases and asked to answer questions similar to the in-class case studies (lectures 17-26). You will receive the questions following the last class and it is due via email by the allotted final exam time period. The exam will be worth 100 points.

**COURSE SCHEDULE AT A GLANCE**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Module | Class | Date | Topic | Lecturer | Exercise |
| Concepts | 1 | Jan 14 | What is genomic epidemiology? | Grubaugh |  |
|  | 2 | Jan 16 | Microbial genetics | Vogels/Grubaugh |  |
| Methods | 3 | Jan 21 | The pathogen sequencing toolbox | Vogels/Grubaugh |  |
|  | 4 | Jan 23 | Molecular basis of NGS | Fauver |  |
|  | 5 | Jan 28 | Clinical metagenomics | Fauver/Grubaugh | #1 |
|  | 6 | Jan 30 | Repositories & alignments | Grubaugh | #2 |
|  | 7 | Feb 4 | Phylogenetics: Basic principles | Brito/Grubaugh |  |
|  | 8 | Feb 6 | Phylogenetics: Building & annotation | Grubaugh/Brito | #3 |
|  | 9 | Feb 11 | Phylogenetics: Nextstrain part 1 | Grubaugh/Brito | #4 |
|  | 10 | Feb 13 | Phylogenetics: Nextstrain part 2 | Brito/Grubaugh |  |
|  | 11 | Feb 18 | Estimating selection pressures | Grubaugh | #5 |
| Applications | 12 | Feb 20 | Integration into public health systems | Grubaugh |  |
|  | 13 | Feb 25 | Pathogen/resistance identification | Grubaugh |  |
|  | 14 | Feb 27 | Outbreak investigation | Grubaugh |  |
|  | 15 | Mar 3 | Investigating epidemic spread | Petrone/Grubaugh |  |
| Recap | 16 | Mar 5 | Discuss exercises | Grubaugh | **All due** |
|  |  | Mar 10 | Spring break |  |  |
|  |  | Mar 12 | Spring break |  |
|  |  | Mar 17 | Spring break |  |
|  |  | Mar 19 | Spring break |  |
| Case studies | 17 | Mar 24 | Unexpected Zika outbreaks | Guests |  |
|  | 18 | Mar 26 | Food-borne outbreaks | Students |  |
|  | 19 | Mar 31 | Vaccine design and evaluation | Guest/Students |  |
|  | 20 | Apr 2 | Plasmodium transmission & resistance | Students |  |
|  | 21 | Apr 7 | HIV emergence & local transmission | Students |  |
|  | 22 | Apr 9 | Ebola virus reemergence & spread | Guest/Students |  |
|  | 23 | Apr 14 | Tracking TB transmission | Guest/Students |  |
|  | 24 | Apr 16 | Zoonotic emergence (**discuss exam**) | Students |  |
|  | 25 | Apr 21 | Hospital outbreaks & drug resistance | Students |  |
|  | 26 | Apr 23 | Clinical metagenomics | Guest/Students |  |
|  |  | Apr 24 | **FINAL EXAM released (take home)** |  |  |
|  |  | May 5 | **FINAL EXAM due (at midnight)** |  |  |

**CLASS TEACHING POINTS, EXERCISES, AND READINGS**

Class 1: What is genomic epidemiology?

* Lecturer: Nathan Grubaugh
* Class structure and teaching points:
  + Fundamental concepts of using pathogen genomics for public health
  + Course learning objectives, overview, expectations, exercises, presentations, and exams

Class 2: Microbial genetics

* Lecturers: Chantal Vogels (Postdoc, YSPH, EMD) & Nathan Grubaugh
* Class structure and teaching points:
  + Genetic code and variation
  + Population dynamics
  + Genetics/genomics of viruses, bacteria, and parasites
  + How we use microbial evolution for epidemiology
* Before class:
  + Read: (The-Phylogenetic-Handbook) - Chapter 1: *Basic concepts of molecular evolution*

Class 3: The pathogen sequencing toolbox

* Lecturers: Chantal Vogels (Postdoc, YSPH, EMD) & Nathan Grubaugh
* Class structure and teaching points:
  + What is next-generation sequencing?
  + Sequencing approaches and platforms
  + How to match a method with a question
  + Class activity: Sequencing approaches for mock scenarios
* Before class:
  + Read: (Class-3\_McElroy-et-al\_2014.pdf) *Deep sequencing of evolving pathogen populations: applications, errors, and bioinformatic solutions*
  + Read: (Class-3\_Maccannell\_2018.pdf) *Platforms and Analytical Tools Used in Nucleic Acid Sequence-Based Microbial Genotyping Procedures*

Class 4: Molecular basis of next-generation sequencing

* Lecturers: Joseph Fauver (Postdoc, YSPH, EMD)
* Class structure and teaching points:
  + Overview of Nanopore MinION sequencing (*in vivo*!)
  + Basic principles for preparing microbial RNA or DNA for sequencing
  + What is the difference between Nanopore and Illumina sequencing?
  + Computational approaches for processing and analyzing NGS data
  + Primer on quality control
  + Examples of data generation & processing for specific questions
* Before class:
  + Watch: Nanopore sequencing - https://www.youtube.com/watch?v=E9-Rm5AoZGw
  + Watch: Illumina sequencing - <https://www.youtube.com/watch?v=womKfikWlxM>
  + Read: (Class-4\_Eisenhofer-et-al\_2109) *Contamination in Low Microbial Biomass Microbiome Studies: Issues and Recommendations*

Class 5: Clinical metagenomics

* Lecturers: Joseph Fauver (Postdoc, YSPH, EMD) & Nathan Grubaugh
* Class structure and teaching points:
  + What is metagenomics (and clinical metagenomics)?
  + Applications, opportunities, challenges, and future of clinical metagenomics
  + Intro to IDSeq and other analysis software
  + Start Exercise #1: Metagenomic analysis using IDseq
  + Sign up for presentations
* Before class:
  + **Read**: (Exercise-1.doc) Metagenomic analysis using IDseq
  + **Sign-up for IDseq account (will receive email)**: <https://idseq.net/>
  + Read: (Class-5\_Gu-et-al\_2019.pdf) *Clinical metagenomic next-generation sequencing for pathogen detection*

Class 6: Repositories & alignments

* Lecturer: Nathan Grubaugh
* Class structure and teaching points:
  + Overview of NGS data to phylogenetics workflow
  + Reference guided alignments
  + Reconstructing consensus genomes
  + Examples of public repositories for pathogen sequences (and metadata)
  + Primer on the importance of complete metadata and informative headers
  + Multiple sequence alignments
  + Start Exercise #2: Public repositories and multi-sequence alignments
  + Sign up for presentations
* Before class:
  + **Download**: UGene - <http://ugene.net/download.html>
  + **Read**: (Excersice-2.doc) Public repositories and multi-sequence alignments
  + **Identify**:pathogen (virus or bacteria) and question
    - Review public repositories for data to answer your question (see Class 1 and exercise 2)
  + **Download**: (ZIKV\_test-data.fasta) - Zika virus sequences for in class example of multiple sequence alignments
  + Read: (The-Phylogenetic-Handbook.pdf) - Chapter 2: *Sequence databases and database searching*
  + Read: (The-Phylogenetic-Handbook.pdf) - Chapter 3: *Multiple sequence alignment*

Class 7: Phylogenetics: Basic principles

* Lecturers: Anderson Brito (Postdoc, YSPH, EMD) & Nathan Grubaugh
* Class structure and teaching points:
  + Types of phylogenetic trees & reading trees
  + Overview of phylogenetic methods (Parsimony, Distance, Maximum-likelihood, Bayesian)
  + Nucleotide substitution models and molecular clocks
  + Bootstrap analysis to evaluate reliability
* Before class:
  + Read: (The-Phylogenetic-Handbook.pdf) - Chapter 4: *Genetic distances and nucleotide substitution models*
  + Read: (The-Phylogenetic-Handbook.pdf) - Chapter 5: *Phylogenetic inference based on distance methods*
  + Read: (The-Phylogenetic-Handbook.pdf) - Chapter 6: *Phylogenetic inference using maximum likelihood methods*

Class 8: Phylogenetics: Building & annotation

* Lecturers: Nathan Grubaugh & Anderson Brito (Postdoc, YSPH, EMD)
* Class structure and teaching points:
  + Brief review of maximum-likelihood phylogenetics and software
  + Primer on tree rooting, annotation, and polytomies
  + Start Exercise #3: Phylogenetic tree reconstruction
  + Reminders for Exercise #4: Installing Nextstrain
* Before class:
  + **Read**: (Exercise-3.doc) Phylogenetic tree reconstruction
  + **Bring***:* Multi-sequence alignment file (fasta) and UGene project file
  + Read: *How to read a phylogenetic tree*: <http://artic.network/how-to-read-a-tree.html>
  + Read: *Reading trees: A quick review:* <https://evolution.berkeley.edu/evolibrary/article/0_0_0/phylogenetics_02>
  + Read: *Reading trees: Phylogenetic pitchforks*: <https://evolution.berkeley.edu/evolibrary/article/0_0_0/phylogenetics_03>

Class 9: Phylogenetics: Nextstrain part 1

* Lecturers: Nathan Grubaugh & Anderson Brito (Postdoc, YSPH, EMD)
* Class structure and teaching points:
  + Introduction to Nextstrain (Augar, Auspice, TreeTime)
  + Nextstrain “community” builds to promote rapid science communication
  + Start Exercise #4: Interactive phylogenetics using Nextstrain
    - Installing: python3, linux (for Windows users), augar, & auspice
    - Overview of Nextstrain directory
    - Nextstrain build with test data
    - Check build using Auspice
    - Formatting data for Nextstrain (must find coordinates for locations)
* Before class:
  + **Read**: (Exercise-4.doc) Interactive phylogenetics using Nextstrain
  + **Bring***:* Multi-sequence alignment (.fasta) and metadata (.csv) files
  + **Download**: All files needed for the exercise - <https://github.com/grubaughlab/nextstrain_course>
  + Read: - Nextstrain workshop at RIVM - <https://neherlab.org/201910_RIVM_nextstrain.html>
  + Read: Nextstrain documentation - <https://nextstrain.org/docs/getting-started/introduction>
  + Read: (Class-9\_Hadfield-et-al\_2018.pdf) *Nextstrain: real-time tracking of pathogen evolution*
  + Read: (Class-9\_Sagulenko-et-al\_2018.pdf) *TreeTime: Maximum-likelihood phylodynamic analysis*

Class 10: Phylogenetics: Nextstrain part 2

* Lecturers: Anderson Brito (Postdoc, YSPH, EMD) & Nathan Grubaugh
* Class structure and teaching points:
  + Continue Exercise #4: Interactive phylogenetics using Nextstrain
    - Check student dataset formatting
    - Run nextstrain build for student dataset
    - Creating/operating a github repo
    - Make nextstrain build ‘live’ on github
* Before class:
  + **Read**: (Exercise-4.doc) Interactive phylogenetics using Nextstrain
  + **Bring**: Nextstrain formatted data

Class 11: Estimating selection pressures

* Lecturer: Nathan Grubaugh
* Class structure and teaching points:
  + Recap on Nextstrain
  + Why do we care about selection/adaptation from an epidemiological perspective?
  + Basic concepts and molecular footprint of selection
  + Estimating selection pressures (and biases/pitfalls!)
  + Phenotypic verification of bioinformatic results
  + Exercise #5: Estimating selection using Datamonkey
* Before class:
  + **Read**: (Exercise-5.doc) Estimating selection using Datamonkey
  + **Bring**: Multi-sequence alignment file (fasta)
  + **Download**: (Test-data\_trimmed-alignment.fasta) - Zika virus alignment for in class example of running Datamonkey
  + Read: (The-Phylogenetic-Handbook.pdf) - Chapter 13: *Natural selection and adaptation of molecular sequences*
  + Read: (The-Phylogenetic-Handbook.pdf) - Chapter 14: *Estimating selection pressures on alignments of coding sequences*
  + Web resource: <https://www.datamonkey.org/>

Class 12: Integration into public health systems

* Lecturer: Nathan Grubaugh
* Class structure and teaching points:
  + Attributes of genomics that drive adoption into public health
  + Examples of successful systems
  + Challenges of integration into a structured surveillance system
  + Importance of collaborations and training programs
  + Additional data sources (‘meta science or systems epidemiology’)
  + Considerations for resource limited regions
  + Group activity: Aligning interests, roles, and outcomes (academic, public health, politician, general public)
  + Exercises: open discussion (last 10-30m of class)
* Before class:
  + Read: (Class-12\_Armstrong-et-al\_2019.pdf) *Pathogen genomics in public health*
  + Read: (Class-12\_Gardy-Loman\_2018.pdf) *Towards a genomics-informed, real-time, global pathogen surveillance system*

Class 13: Pathogen/resistance identification

* Lecturer: Nathan Grubaugh
* Class structure and teaching points:
  + Identification for clinical (individual) and surveillance (population) purposes
  + Common strategies for pathogen detection/identification (traditional vs genomic)
  + How to determine if the pathogen has a known resistance allele
  + Global epidemic of drug resistance
  + How microbes evolve resistance to drugs
  + Group activity: How to close the surveillance gap
  + Exercises: open discussion (last 10-30m of class)
* Before class:
  + Read: (Class-13\_Ladner-et-al\_2019.pdf) *Precision epidemiology for infectious disease control*
  + Read: (Class-13\_Clutter-et-al\_2016.pdf) *HIV-1 drug resistance and resistance testing*
  + Read: (Class-13\_Khan-et-al\_2019.pdf) *Current and emerging methods of antibiotic susceptibility testing*

Class 14: Outbreak investigation

* Lecturer: Nathan Grubaugh
* Class structure and teaching points:
  + Genomic applications during outbreaks
  + Reading a phylogenetic tree: Pathogen introductions, origins, and dynamics
  + Importance of open science and communication
  + Primer on hospital outbreaks
  + Group activity: Investigating an outbreak using NextStrain
  + Exercises: open discussion (last 10-30m of class)
* Before class:
  + Read: (Class-14\_Grubaugh-et-al\_2019.pdf) *Tracking virus outbreaks in the twenty-first century*
  + Read: (Class-14\_Popovich-Snitkin\_2017.pdf) *Whole genome sequencing – implications for infection prevention and outbreak investigations*
  + Read: (Class-14\_Yozwiak-et-al\_2015.pdf) *Data sharing: make outbreak research open access*
  + Read: (Class-14\_Peacock-et-al\_2018.pdf) *Changing the paradigm for hospital outbreak detection by leading with genomic surveillance of nosocomial pathogens*
  + Activity: <https://nextstrain.org/community/grubaughlab/DENV-genomics/DENV1-Brazil>

Class 15: Investigating epidemic spread

* Lecturers: Mary Petrone (PhD student, YSPH, EMD) & Nathan Grubaugh
* Class structure and teaching points:
  + Genomics to dissect spatial structure and dynamics of spread
  + Effects of surveillance and sampling biases
  + Integration and testing predictors of spread
  + Applications for control efforts (vaccine/drug design & placement)
  + Analysis and visualization tools
  + Group activity: Mock WHO recommendation for flu vaccine
  + Exercises: open discussion (last 10-30m of class)
* Before class:
  + Read: (Class-15\_Faria-et-al\_2011.pdf) *Towards a quantitative understanding of viral phylogeography*
  + Read: (Class-15\_Baele-et-al\_2017.pdf) *Emerging Concepts of Data Integration in Pathogen Phylodynamics*
  + Read: (Class-15\_Baele-et-al\_2018.pdf) *Recent advances in computational phylodynamics*
  + Read: (Class-15\_Bedford-et-al\_2019.pdf) *Seasonal influenza circulation patterns and projections for September 2019 to September 2020*
  + Activity: <https://nextstrain.org/flu/seasonal/h3n2/ha/2y>

Class 16:Discuss exercises

* Lecturer: Nathan Grubaugh
* Class structure and teaching points:
  + Review “Medical Detectives” IDseq findings
  + Interesting selection findings
  + How well do the UGene trees match the Nextstrain trees?
  + Informal Nextstrain presentations
* Before class:
  + **Email exercises to TF before class**
  + Be prepared to discuss your findings

**Classes 17-26: Case studies**

* Student and guest presentations of published genomic epidemiology studies to understand real-world applications for a variety of pathogens and questions.
* Read: (2020\_EMD-531\_Presentations-overview.pdf)
* **It is very important to read each paper even if you are not presenting as you may be asked to participate during class.**

Class 17: Unexpected Zika outbreaks

* Presentation 1 – **Sarah Hill, Postdoc, University of Oxford**:
  + (Class-17\_Hill-et-al\_2019.pdf) *Emergence of the Asian lineage of Zika virus in Angola: an outbreak investigation*
* Presentation 2 – **Nathan Grubaugh, Assistant Professor, YSPH, EMD**:
  + (Class-17\_Grubaugh-et-al\_2017.pdf) *Genomic epidemiology reveals multiple introductions of Zika virus into the United States*

Class 18: Food-borne outbreaks

* Presentation 1 - **Students**:
  + (Class-18\_Jackson-et-al\_2016) *Implementation of Nationwide Real-time Whole-genome Sequencing to Enhance Listeriosis Outbreak Detection and Investigation*
* Presentation 2 - **Students**:
  + (Class-18\_Baker-et-al\_2017.pdf) *Whole genome sequencing of Shigella sonnei through PulseNet Latin America and Caribbean: advancing global surveillance of foodborne illnesses*

Class 19: Vaccine design and evaluation

* Presentation 1 – **Dan Weinberger, Associate Professor, YSPH, EMD**:
  + (Class-19\_Masignani-et-al\_2019.pdf) *The development of a vaccine against meningococcus B using reverse vaccinology*
* Presentation 2 - **Students**:
  + (Class-19\_Potter-et-al\_2019.pdf) *Evolution and rapid spread of a reassortant A(H3N2) virus that predominated the 2017–2018 influenza season*

Class 20: Plasmodium transmission & resistance

* Presentation 1 - **Students**:
  + (Class-20\_Daniels-et-al\_2015.pdf) *Modeling malaria genomics reveals transmission decline and rebound in Senegal*
* Presentation 2 - **Students**:
  + (Class-20\_MalariaGen\_2016.pdf) *Genomic epidemiology of artemisinin resistant malaria*

Class 21: HIV emergence & local transmission

* Presentation 1 - **Students**:
  + (Class-21\_Worobey-et-al\_2016.pdf) *1970s and ‘Patient 0’ HIV-1 genomes illuminate early HIV/AIDS history in North America*
* Presentation 2 - **Students**:
  + (Class-21\_Poon-et-al\_2016.pdf) *Near real-time monitoring of HIV transmission hotspots from routine HIV genotyping: an implementation case study*

Class 22: Ebola virus reemergence & spread

* Presentation 1 - **Students**:
  + (Class-22\_Dudas-et-al\_2017.pdf) *Virus genomes reveal factors that spread and sustained the Ebola epidemic*
* Presentation 2 – **Allison Black, PhD student, University of Washington/Fred Hutch**:
  + Paper TBD

Class 23: Tracking TB transmission

* Presentation 1 – **Chongguang Yang, Postdoc, YSPH, EMD**:
  + (Class-23\_Yang-et-al\_2017.pdf) *Transmission of multidrug-resistant Mycobacterium tuberculosis in Shanghai, China: a retrospective observational study using whole-genome sequencing and epidemiological investigation*
* Presentation 23 - **Students**:
  + (Class-18\_Gardy-et-al\_2011.pdf) *Whole-Genome Sequencing and Social Network Analysis of a Tuberculosis Outbreak*

Class 24: Zoonotic emergence

* Presentation 1 - **Students**:
  + (Class-24\_Kafetzopoulou-et-al\_2019.pdf) *Metagenomic sequencing at the epicenter of the Nigeria 2018 Lassa fever outbreak*
* *Only one presentation this class.* 
  + Second half will be a discussion about the final exam.

Class 25: Hospital outbreaks & drug resistance

* Presentation 1 - **Students**:
  + (Class-25\_Sullivan-et-al\_2019.pdf) *A Complete Genome Screening Program of Clinical Methicillin Resistant Staphylococcus aureus Isolates Identifies the Origin and Progression of a Neonatal Intensive Care Unit Outbreak*
* Presentation 2 - **Students**:
  + (Class-25\_Harris-et-al\_2013.pdf) *Whole-genome sequencing for analysis of an outbreak of meticillin-resistant Staphylococcus aureus: a descriptive study*

Class 26: Clinical metagenomics

* Presentation 1 - **Students**:
  + (Class-26\_Wilson-et-al\_2019.pdf) *Clinical Metagenomic Sequencing for Diagnosis of Meningitis and Encephalitis*
* Presentation 2 – **Joseph Fauver, Postdoc, YSPH, EMD**:
  + (Class-26\_Saha-et-al\_2019.pdf) *Unbiased metagenomic sequencing for pediatric meningitis in Bangladesh reveals neuroinvasive Chikungunya virus outbreak and other unrealized pathogens*